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| 10/573,381 | 03/24/2006 | Jun Tomono | TOMONO 5 | 9348 |

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| EXAMINER | |
|---|---|
| RAMIREZ, DELIA M | |

| ART UNIT | PAPER NUMBER |
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| 1652 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/573,381 | TOMONO ET AL. | |
| | Examiner | Art Unit | |
| | Delia M. Ramirez | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *9-13,16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/06,3/2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *alignments*.

## DETAILED ACTION

### *Status of the Application*

Claims 1-17 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's preliminary amendment of claims 5, 8-9, 11, 14-15 as submitted in a communication filed on 3/24/2006 is acknowledged.

Applicant's election of Group I, claims 1-8, 14 drawn to a polypeptide having RNase III activity and a composition comprising said polypeptide, as submitted in a communication filed on 4/7/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, claim 15, which is directed to a kit for degrading a dsRNA which comprises an RNase III polypeptide will be rejoined for examination as it is deemed an obvious variation of the elected invention. The kit of claim 15 is essentially a product which comprises the elected protein. Therefore, the restriction requirement between Groups I and III as set forth in the Office action mailed on 3/5/2008 is hereby withdrawn.

Claims 9-13, 16-17 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1-8, 14 and 15 are at issue and are being examined herein.

### *Specification*

1. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, for example, page 4, line 18. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

2. The abstract is objected to since it does not appear to be written in proper idiomatic English. Appropriate correction is required.

***Priority***

3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to JAPAN 2003-342260 filed on 09/30/2003, and JAPAN 2003-409638 filed on 12/08/2003. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. No certified English translation of the foreign priority documents has been submitted.

4. This application is the US national stage of PCT/JP04/14255 filed on 09/29/2004.

***Information Disclosure Statement***

5. The information disclosure statements (IDS) submitted on 6/20/2006 and 3/2/2007 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the Examiner.

***Claim Objections***

6. Claims 1, 14, 15 are objected to due to the recitation of " which is derived from....and with which a dsRNA....complete degradation". To enhance clarity, the term should be amended to recite, for example, "wherein said polypeptide is derived from a microorganism, and wherein complete degradation of dsRNA with said polypeptide can result in a dsRNA degradation product that is effective for RNA interference". Appropriate correction is required.

7. Claim 2 is objected to due to the recitation of "for which reaction conditions .....can be obtained". To enhance clarity, the term should be amended to recite, for example, "wherein degradation

of dsRNA with said polypeptide….. results in a dsRNA degradation product which can be larger than the degradation product obtained by degradation of …..". Appropriate correction is required.

8. Claim 3 is objected to due to the recitation of "of which the dsRNA degradation velocity….can be readily controlled". To enhance clarity, the term should be amended to recite, for example, "wherein the dsRNA degradation velocity of said polypeptide…is slower than the …of". Appropriate correction is required.

9. Claim 4 is objected to due to the recitation of "of which the dsRNA degradation velocity is slower….about 10 pairs". To enhance clarity, the term should be amended to recite, for example, "wherein the dsRNA degradation velocity of said polypeptide….is slower than the…, and wherein said polypeptide does not tend to produce...". Appropriate correction is required.

10. Claim 7 is objected to due to the recitation of "with which a dsRNA…can be obtained". To enhance clarity, it is suggested the term be amended to recite, for example, "wherein degradation of dsRNA with said polypeptide ….results in a dsRNA degradation product which can be larger than the degradation product obtained by degradation of ….". Appropriate correction is required.

11. Claims 14 and 15 are objected to because they are dependent upon a non-elected claim, i.e., 9. For examination purposes, the examiner will assume that these claims are independent claims. Claim 14 will be interpreted as being directed to a composition comprising a polypeptide having RNase III activity, wherein said polypeptide is derived from a microorganism, and wherein complete degradation of dsRNA with said polypeptide results in a dsRNA degradation product that is effective for RNA interference. Claim 15 will be interpreted as being directed to a kit comprising a polypeptide having RNase III activity, wherein said polypeptide is derived from a microorganism, and wherein complete degradation of dsRNA with said polypeptide results in a dsRNA degradation product that is effective for RNA interference. Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

12. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

13. Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-8, as written, do not sufficiently distinguish over proteins as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 US 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as taught by pages 39-41 (paragraphs [065]-[067]) of the specification. See MPEP 2105.

***Claim Rejections - 35 USC § 112, Second Paragraph***

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 2-4, 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

16. Claims 2-4 are indefinite in the recitation of "for which reaction conditions can be readily controlled" for the following reasons. As known in the art, reaction conditions such as temperature, pressure, pH, ionic strength can be readily controlled. Therefore, it is unclear as to how this limitation further limits the claims. For examination purposes, no patentable weight will be given to this term.

17. Claims 2 and 7 are indefinite in the recitation of "larger than a final degradation product obtained by treating a dsRNA with an RNase III from *Escherichia coli*" for the following reasons. The term is

unclear and confusing because the basis for comparison is variable, thus making the determination as whether prior art anticipates the claims impossible. As written, the comparison can be made with different degradation products produced by treating different dsRNA molecules under different conditions and with different RNases III from *Escherichia coli*. A reference can be at the same time anticipatory and non-anticipatory depending on what is used as the basis for comparison. For example, prior art may meet the recited limitations if the *E. coli* RNase III is contacted with a dsRNA molecule X under conditions X but may fail to meet the limitations recited if the *E. coli* RNase III is contacted with a dsRNA molecule Y under conditions Y. Similarly, prior art may meet the recited limitations if the *E. coli* RNase III is X but may fail to meet the limitations recited if the *E. coli* RNase III is Y. For examination purposes, no patentable weight will be given to the term. Correction is required.

18. Claims 3 and 4 are indefinite in the recitation of "the dsRNA degradation velocity is slower than the dsRNA degradation velocity of an RNase III from *Escherichia coli*" for the following reasons. The term is unclear and confusing because the basis for comparison is variable, thus making the determination as whether prior art anticipates the claim impossible. As written, the comparison can be made under different conditions with different dsRNA molecules and different RNases III from *E. coli*. A reference can be at the same time anticipatory and non-anticipatory depending on what is used as the basis for comparison. For example, prior art may meet the recited limitations if the degradation velocity used is one obtained when *E. coli* RNase III is contacted with a dsRNA molecule X under conditions X but may fail to meet the limitations recited if the degradation velocity used is one obtained when *E. coli* RNase III is contacted with a dsRNA molecule Y under conditions Y. Similarly, prior art may meet the recited limitations if the *E. coli* RNase III is X but may fail to meet the limitations recited if the *E. coli* RNase III is Y. For examination purposes, no patentable weight will be given to the term. Correction is required.

19. Claim 7 is indefinite in the recitation of "nucleotide sequence that is capable of hybridizing to the nucleotide sequence of SEQ ID NO: 1 under stringent conditions" for the following reasons. First, as

known in the art, a nucleotide sequence is a graphical representation of the order in which nucleotides are arranged in a polynucleotide. Hybridization is known to occur among polynucleotides. Thus, hybridization does not occur among sequences. In addition, the term "hybridizing…under stringent conditions" is indefinite because it is unclear which polynucleotide is recited absent a statement of the experimental conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. The art does not recognize a single set of experimental conditions as "stringent" and even the specification indicates that there are different degrees of stringency (pages 18-20, paragraphs [033]-[034]). The specification, while providing some conditions which are labeled as "stringent", does not define the conditions which are considered stringent. For examination purposes, it will be assumed that the term "a nucleotide sequence that is capable of hybridizing to the nucleotide sequence of SEQ ID NO: 1 under stringent conditions" reads "the nucleotide sequence of a nucleic acid which hybridizes to the polynucleotide of SEQ ID NO: 1 under any hybridization conditions". Correction is required.

***Claim Rejections - 35 USC § 112, First Paragraph***

20. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

21. Claims 1-8, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-7, 14 and 15 require a genus of proteins comprising any structure (i.e., sequence), wherein said proteins have RNase III activity. Claim 8 is directed to a fusion protein comprising the

polypeptide of claim 1 fused to any protein which can bind to any nucleic acid. It should be noted that the term "derived from a microorganism" does not further limit the source or structure of the protein recited for the following reasons. A protein derived from a microorganism can be a protein which was initially isolated from a microorganism and was further modified. Since a polypeptide is defined by its structural/functional characteristics, if a protein which was first isolated from microbe X is mutated to have sequence Y, and a protein isolated from organism Z also has the same sequence Y, one of skill in the art could not differentiate between both proteins. As such, the limitation "derived form a microorganism" is not deemed further limiting as it relates to source or structure. With regard to limitations regarding the size of the dsRNA degradation product and its ability to be effective for RNA interference, it is noted that the claims recite "can be obtained" and "does not tend", thus making these limitations optional. With regard to claim 7, it is noted that claim 7 allows the protein to have any structure due to the fact that item (b) recites that the polypeptide can be a variant of the polypeptide of SEQ ID NO: 4 having any number of modifications. See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are

representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

There is no actual structural limitation with regard to the members of the genus of proteins recited. While the specification in the instant application discloses the structure of a single RNase III isolated from a *Shewanella* strain (i.e., SEQ ID NO: 4), the specification provides no clue as to the structural elements required in any protein having the recited RNase III activity, nor does it teach which structural elements within the polypeptide of SEQ ID NO: 4 are required in any protein having the recited RNase III activity. Furthermore, the specification is silent with regard to the structural features required in any RNase III such that it can produce dsRNA degradation products of a certain size, or which structural features are required such that it would display an RNase III activity which is different from that of an *E. coli* RNase III. No information has been provided as to the structural features required in any protein that binds any nucleic acid such that when fused with a protein having RNase III activity, it can degrade dsRNA into fragments having the desired size.

The claim encompass a large genus of proteins which is structurally unrelated. A sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their amino acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. However, in the instant case, there is no structural feature which is representative of all the members of the genus of proteins recited in the claims, and there is no information as to a correlation between structure and function. Furthermore, while one could argue that SEQ ID NO: 4 is representative of the structure of all the members of the genus, such that the recited genus of polypeptides is adequately described, it is noted that the art teaches several examples of how even small structural variability can lead to changes in enzymatic function. For example, Witkowski et al. (Biochemistry 38:11643-11650, 1999) teach that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and

completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teach that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, thus having different function. Therefore, since minor structural changes to a polypeptide may result in changes affecting function, and no additional information correlating structure with the recited activity has been provided, one cannot reasonably conclude that the protein of SEQ ID NO: 4 is representative of the structure of all proteins having the RNase III activity as claimed.

Due to the fact that the specification only discloses a single protein having RNase III activity, and the lack of description of any additional species by any relevant, identifying characteristics or properties, one of skill in the art would not recognize from the disclosure that Applicant was in possession of the claimed invention.

22. Claims 1-8, 14 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 4, as well as a composition and a kit comprising said polypeptide, does not reasonably provide enablement for any protein having RNase III activity, a composition or a kit comprising said protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2nd 1400 (Fed. Cir. 1988)) as follows: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The factors which have lead the Examiner to conclude that the specification fails to teach how to make and/or use the claimed invention without undue experimentation, are addressed in detail below.

***The breath of the claims***. Claims 1-8, 14 and 15 are so broad as to encompass (1) a protein having any structure and RNase III activity, and (2) a composition/kit comprising the protein of (1). See Claim Rejections under 35 USC 112, second paragraph, for claim interpretation. The enablement provided is not commensurate in scope with the claims due to the extremely large number of proteins of unknown structure encompassed by the claims. In the instant case, the specification enables a protein comprising/consisting of SEQ ID NO: 4.

***The amount of direction or guidance presented and the existence of working examples.*** The specification discloses the amino acid sequence of a single RNase III as a working example (SEQ ID NO: 4). However, the specification fails to provide any clue as to the structural elements required in any protein having RNase III activity, or which are the structural elements in the polypeptide of SEQ ID NO: 4 which are essential for any protein to display the desired RNase III activity. No correlation between structure and function has been presented. There is no information or guidance as to which amino acid residues in the polypeptide of SEQ ID NO: 4 can be modified and which ones are to be conserved to create a variant displaying the same activity as that of the polypeptide of SEQ ID NO: 4. There is no disclosure of the structural features associated with the ability to degrade dsRNA into fragments having the desired size, nor there is disclosure of the structural features required in any RNase III such that it would display an RNase III activity which is different from that of an *E. coli* RNase III. In addition, there is no information in the specification or the prior art regarding the structural features required in any nucleic acid binding domain such that when combined with a protein having RNase III activity, it can degrade dsRNA into fragments of a particular length.

***The state of prior art, the relative skill of those in the art, and the predictability or unpredictability of the art.*** The amino acid sequence of a polypeptide determines its structural and

functional properties. While the art discloses several proteins having RNase III activity, neither the specification nor the art provide a correlation between structure and RNase III activity such that one of skill in the art can envision the structure of any RNase III which can degrade dsRNA into fragments having the desired size, or any RNase III which has an enzymatic activity which is different to that of an *E. coli* RNase III. In addition, the art does not provide any teaching or guidance as to (1) which changes can be made to the protein of SEQ ID NO: 4 such that the resulting variants would display the same activity, or (2) the general tolerance of proteins having RNase III activity to structural modifications and the extent of such tolerance. The art clearly teaches that modification of a protein's amino acid sequence to obtain the desired activity without any guidance/knowledge as to which amino acids in a protein are tolerant of modification and which ones are conserved is highly unpredictable. At the time of the invention there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity. For example, Branden et al. (Introduction to Protein Structure, Garland Publishing Inc., New York, page 247) teach that (1) protein engineers are frequently surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes, (2) the often surprising results obtained by experiments where single mutations are made reveal how little is known about the rules of protein stability, and (3) the difficulties in designing *de novo* stable proteins with specific functions. The teachings of Branden et al. are further supported by the teachings of Witkowski et al. (Biochemistry 38:11643-11650, 1999) and Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) already discussed above, where it is shown that even small amino acid changes result in enzymatic activity changes.

***The quantity of experimentation required to practice the claimed invention based on the teachings of the specification.*** While methods of generating or isolating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen by a trial and error process for all polypeptides having the recited activity. Furthermore, in view of the absence of guidance

as to the structural features required in any protein having a nucleic acid binding domain such that when combined with any protein having RNase III activity, one could obtain dsRNA fragments of an specified length, one of skill in the art would have to test an infinite number of combinations to determine which combination of proteins can be used to obtain the desired length. In the absence of (1) a rational and predictable scheme for modifying any residue in the polypeptide of SEQ ID NO: 4 such that the resulting variants would maintain the same RNase III activity, (2) some knowledge or guidance as to the structural features associated with the recited activity such that one could isolate/test only those most likely to have the desired activity, (3) some knowledge or guidance as to which nucleic acid domains can be combined with a protein having RNase III activity such that dsRNA fragments of a particular length can be obtained, and/or (4) a correlation between structure and the recited RNase III activity, one of skill in the art would have to test an essentially infinite number of proteins to determine which ones have the desired activity.

Therefore, taking into consideration the extremely broad scope of the claim, the lack of guidance, the amount of information provided, the lack of knowledge about a correlation between structure and the desired function, and the high degree of unpredictability of the prior art in regard to structural changes and their effect on function, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to practice the claimed invention. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

***Claim Rejections - 35 USC § 102***

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 1-8 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Heidelberg et al. (protein disclosed in GenBank accession number AAN54413, October 23, 2002; DNA disclosed in GenBank accession number AE015579, December 2, 2002).

Claims 1-7 and 14 are directed in part to a polypeptide having RNase III activity and isolated from a *Shewanella* strain. Claim 8 is directed to a fusion protein having RNase III activity and an activity of binding to a nucleic acid. See Claim Rejections under 35 USC 112, first and second paragraphs, for claim interpretation and discussion of scope. Heidelberg et al. teach an RNase III isolated from *Shewanella oneidensis* MR-1 (See entry for Features/source/protein in GenBank submission). The polypeptide of Heidelberg et al. is 85.4% sequence identical to the polypeptide of SEQ ID NO: 4 (85.4% = 193x100/226; 193 matches). See attached alignments. The polynucleotide encoding the protein of Heidelberg et al. is 75.7% sequence identical to the polynucleotide of SEQ ID NO: 1 and would hybridize to the polynucleotide of SEQ ID NO: 1 under certain hybridization conditions. Since an RNase III would degrade dsRNA, the polypeptide of Heidelberg et al. would also degrade dsRNA. Also, as known in the art, RNase III proteins contain a nucleic acid binding domain. Therefore, the teachings of Heidelberg et al. anticipate the instant claims as written/interpreted.

25. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Trotta et al. (Cancer Cell 3(2):145-160, February 2003). Trotta et al. teach a kit comprising an *E. coli* RNase III sold commercially by AMBION (MEGAScript RNAi) for generating siRNA by digesting a 300 bp dsRNA for La gene (page 158, left column, Inhibition of La expression by RNA interference). Claim 15 as interpreted is directed to a kit comprising a protein having RNase III activity. See Claim Rejections under 35 USC 112 first and second paragraph, for claim interpretation and discussion of scope. Therefore the AMBION kit taught by Trotta et al. anticipates the instant claim as written/interpreted.

***Allowable Subject Matter***

26. The polypeptide of SEQ ID NO: 4 appears to be allowable over the prior art of record.

***Conclusion***

27. No claim is in condition for allowance.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 9:30:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Nashaat Nashed can be reached on (571) 272-0934. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

/Delia M. Ramirez/

Delia M. Ramirez, Ph.D.
Primary Patent Examiner
Art Unit 1652

DR
July 29, 2008